

Serial No. 10/724,233
Atty. Docket No.: P63882US1

Listing of Claims:

1-83 (canceled).

84. (Previously presented) A method of solid phase peptide synthesis for preparing a ligand presenting assembly (LPA) for presentation of at least two identical peptide sequences having between 4 and 20 amino acids and having free C-terminal groups comprising the steps of:

a) assembling a plurality of identical, fully side-chain protected peptide sequences on a single solid phase resin support to provide a compound having the following formula:



wherein S represents the solid phase resin support, A represents a peptide sequence having between 4 and 20 naturally occurring L-amino acid residues, and a is ≥ 2 , and represents the number of fully side-chain protected peptide sequences on the resin support;

b) deprotecting any protected N-terminal amino groups while the peptide sequences are still attached to the resin support;

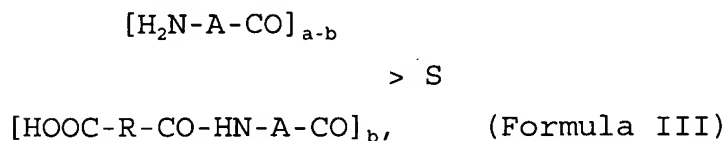
c) reacting the resulting compound having unprotected N-terminal amino groups in the peptide sequences with between 0.4 and 0.6 equivalents of an achiral dicarboxylic acid selected from the group consisting of: imino diacetic acid, 2-amino malonic acid, malonic acid, 3-amino glutaric acid and glutaric acid, being

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Fmoc, Boc or Aloc-protected on the amino or imino group, if present, thus having the following formula:



wherein R represents a $N(X)(CH_2-)_2$, $NH(X)CH<$, $CH_2<$, $NH(X)CH(CH_2-)_2$ or $CH_2(CH_2-)_2$ group, and X represents an Fmoc, Boc or Aloc group, so that between 0.4 and 0.6 equivalents of said achiral dicarboxylic acid are added for every 1 equivalent of unprotected N-terminal amino group resulting in a compound with the following formula:



wherein b is between about 0.4a and 0.6a;

d) activating the product of step (c) (Formula III) so that the free carboxylic acid group reacts with the free N-terminal amino group; resulting in a compound of the following formula:



and

e) optionally splitting of any N-terminal Fmoc-group, Boc-group or Aloc-group;

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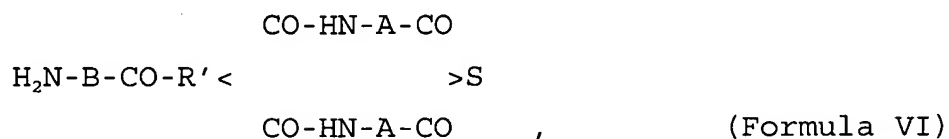
f) cleaving the product of step (e) from the resin support resulting in a LPA peptide sequence having the following formula:



wherein, if N is present in R, X represents H, an Fmoc, Boc or Alloc group, and Y is OH or NH₂.

85. (Previously presented) A method according to claim 84 further comprising the steps of prior to step (f)

(e') splitting of any N-terminal Fmoc, Boc or Alloc group originating from the dicarboxylic acid used in step (c) and (e'') continuing the solid phase synthesis so as to provide a compound of the following formula:



wherein B represents a peptide sequence, and R' represents a N(CH₂-)₂, NHCH<, or NHCH(CH₂-)₂ group.

86. (Previously presented) The method according to claim 84, wherein the achiral acid is imino diacetic acid.

87. (Currently amended) The method according to claim ~~84~~ 91, wherein the peptide sequences are derived from OspC protein of *Borrelia burgdorferi*.

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88. (Currently amended) The method according to claim ~~84~~ 91 for preparing an LPA for presenting two identical C-terminal sequences Pro-Lys-Lys-Pro (Seq. ID 7) of OspC.

89. (Currently amended) The method according to claim ~~84~~ 91, wherein the peptide sequences are derived from the flagellum of *Borrelia burgdorferi*.

90. (Currently amended) The method according to claim ~~84~~ 91 for preparing an LPA selected from the group consisting of

[LPA-I]: $\text{FmocN}(\text{CH}_2\text{CO-ProValValAlaGluSerProLysLysPro-OH})_2$
($\text{FmocN}(\text{CH}_2\text{CO-Seq. ID 1-OH})_2$)

[LPA-III]: $\text{NH}_2\text{CH}(\text{CH}_2\text{CO-ProValValAlaGluSerProLysLysPro-OH})_2$
($\text{NH}_2\text{CH}(\text{CH}_2\text{CO-Seq. ID 1-OH})_2$)

[LPA-VII]: $\text{CH}_2(\text{CH}_2\text{CO-}\beta\text{-Ala-}\beta\text{-AlaLysGluProAsnLysGlyValAsnProAspGluVal}\beta\text{-Ala})_2$ ($\text{CH}_2(\text{CH}_2\text{CO-}\beta\text{-Ala-}\beta\text{-Ala-Seq. ID 4-}\beta\text{-Ala-OH})_2$)₂

[LPA-VIII]: $\text{H}_2\text{C}(\text{CH}_2\text{CO-LysGluProAsnLysGlyValAsnProAspGluVal}\beta\text{Ala})_2\text{COOH}$ ($\text{H}_2\text{C}(\text{CH}_2\text{CO-Seq. ID 4-}\beta\text{-Ala})_2\text{COOH}$),

[LPA-IX]: $\text{Fmoc-NHCH}(\text{CH}_2\text{CO-AspArgValTyrIleHisProPheHisLeu-NH}_2)_2$
($\text{Fmoc-NHCH}(\text{CH}_2\text{CO-Seq. ID 5-NH}_2)_2$),

[LPA-X]: $\text{Aloc-NHCH}(\text{CH}_2\text{CO-AspArgValTyrIleHisProPheHisLeu-NH}_2)_2$
($\text{Aloc-NHCH}(\text{CH}_2\text{CO-Seq. ID 5-NH}_2)_2$), and

91. (Previously presented) A method of solid phase peptide synthesis for preparing a ligand presenting assembly (LPA) for presentation of at least two identical peptide sequences from *Borrelia burgdorferi* having between 4 and 20 amino acids and having free C-terminal groups comprising the steps of:

a) assembling a plurality of identical, fully side-chain protected peptide sequences on a single solid phase resin support to provide a compound having the following formula:



wherein S represents the solid phase resin support, A represents a peptide sequence having between 4 and 20 naturally occurring L-amino acid residues, and a is ≥ 2 , and represents the number of fully side-chain protected peptide sequences on the resin support;

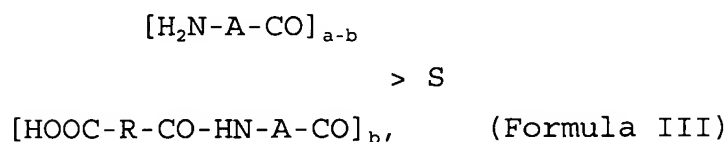
b) deprotecting any protected N-terminal amino groups while the peptide sequences are still attached to the resin support;

c) reacting the resulting compound having unprotected N-terminal amino groups in the peptide sequences with between 0.4 and 0.6 equivalents of an achiral dicarboxylic acid selected from the group consisting of: imino diacetic acid, 2-amino malonic acid, malonic acid, 3-amino glutaric acid and glutaric acid, being Fmoc, Boc or Alloc-protected on the amino or imino group, if present, thus having the following formula:



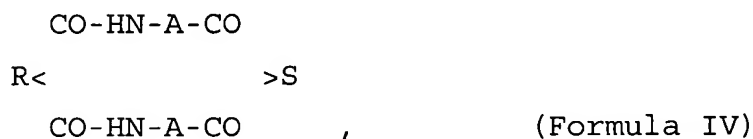
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wherein R represents a $N(X)(CH_2-)_2$, $NH(X)CH<$, $CH_2<$, $NH(X)CH(CH_2-)_2$ or $CH_2(CH_2-)_2$ group, and X represents an Fmoc, Boc or Alloc group, so that between 0.4 and 0.6 equivalents of said achiral dicarboxylic acid are added for every 1 equivalent of unprotected N-terminal amino group resulting in a compound with the following formula:



wherein b is between about 0.4a and 0.6a;

d) activating the product of step (c) (Formula III) so that the free carboxylic acid group reacts with the free N-terminal amino group; resulting in a compound of the following formula:



and

e) optionally splitting of any N-terminal Fmoc-group, Boc-group or Alloc-group;

f) cleaving the product of step (e) from the resin support resulting in a LPA peptide sequence having the following formula:



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wherein, if N is present in R, X represents H, an Fmoc, Boc or Alloc group, and Y is OH or NH₂.

92. (Previously presented) A method of solid phase peptide synthesis for preparing a ligand presenting assembly (LPA) for presentation of at least two identical peptide sequences derived from OspC protein of *Borrelia burgdorferi* having between 4 and 20 amino acids and having free C-terminal groups comprising the steps of:

a) assembling a plurality of identical, fully side-chain protected peptide sequences on a single solid phase resin support to provide a compound having the following formula:



wherein S represents the solid phase resin support, A represents a peptide sequence having between 4 and 20 naturally occurring L-amino acid residues, and a is ≥ 2 , and represents the number of fully side-chain protected peptide sequences on the resin support;

b) deprotecting any protected N-terminal amino groups while the peptide sequences are still attached to the resin support;

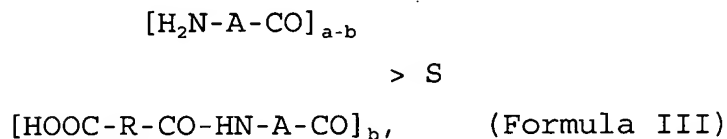
c) reacting the resulting compound having unprotected N-terminal amino groups in the peptide sequences with between 0.4 and 0.6 equivalents of an achiral dicarboxylic acid selected from the group consisting of: imino diacetic acid, 2-amino malonic acid, malonic acid, 3-amino glutaric acid and glutaric acid, being

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Fmoc, Boc or Aloc-protected on the amino or imino group, if present, thus having the following formula:



wherein R represents a $N(X)(CH_2-)_2$, $NH(X)CH<$, $CH_2<$, $NH(X)CH(CH_2-)_2$ or $CH_2(CH_2-)_2$ group, and X represents an Fmoc, Boc or Aloc group, so that between 0.4 and 0.6 equivalents of said achiral dicarboxylic acid are added for every 1 equivalent of unprotected N-terminal amino group resulting in a compound with the following formula:



wherein b is between about 0.4a and 0.6a;

d) activating the product of step (c) (Formula III) so that the free carboxylic acid group reacts with the free N-terminal amino group; resulting in a compound of the following formula:

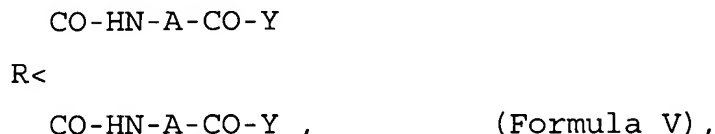


and

e) optionally splitting of any N-terminal Fmoc-group, Boc-group or Aloc-group;

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f) cleaving the product of step (e) from the resin support resulting in a LPA peptide sequence having the following formula:



wherein, if N is present in R, X represents H, an Fmoc, Boc or Alloc group, and Y is OH or NH₂.

93. (Previously presented) A method of solid phase peptide synthesis for preparing a ligand presenting assembly (LPA) for presentation of at least two identical peptide sequences from the flagellum of *Borrelia burgdorferi* having between 4 and 20 amino acids and having free C-terminal groups comprising the steps of:

a) assembling a plurality of identical, fully side-chain protected peptide sequences on a single solid phase resin support to provide a compound having the following formula:



wherein S represents the solid phase resin support, A represents a peptide sequence having between 4 and 20 naturally occurring L-amino acid residues, and a is ≥ 2 , and represents the number of fully side-chain protected peptide sequences on the resin support;

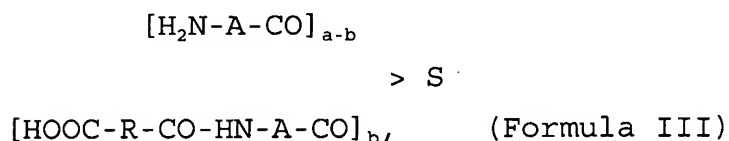
b) deprotecting any protected N-terminal amino groups while the peptide sequences are still attached to the resin support;

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c) reacting the resulting compound having unprotected N-terminal amino groups in the peptide sequences with between 0.4 and 0.6 equivalents of an achiral dicarboxylic acid selected from the group consisting of: imino diacetic acid, 2-amino malonic acid, malonic acid, 3-amino glutaric acid and glutaric acid, being Fmoc, Boc or Aloc-protected on the amino or imino group, if present, thus having the following formula:



wherein R represents a $N(X)(CH_2-)_2$, $NH(X)CH<$, $CH_2<$, $NH(X)CH(CH_2-)_2$ or $CH_2(CH_2-)_2$ group, and X represents an Fmoc, Boc or Aloc group, so that between 0.4 and 0.6 equivalents of said achiral dicarboxylic acid are added for every 1 equivalent of unprotected N-terminal amino group resulting in a compound with the following formula:



wherein b is between about 0.4a and 0.6a;

d) activating the product of step (c) (Formula III) so that the free carboxylic acid group reacts with the free N-terminal amino group; resulting in a compound of the following formula:



and

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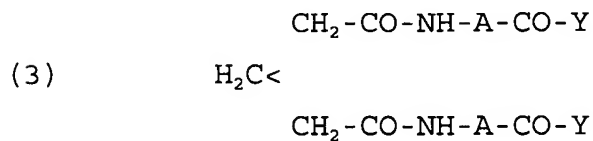
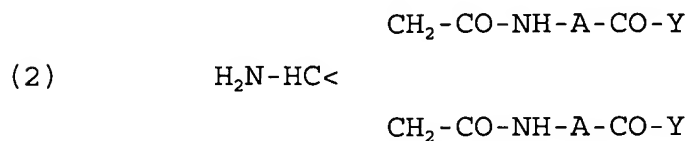
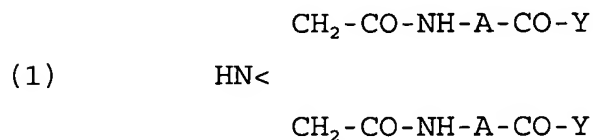
e) optionally splitting of any N-terminal Fmoc-group, Boc-group or Alloc-group;

f) cleaving the product of step (e) from the resin support resulting in a LPA peptide sequence having the following formula:

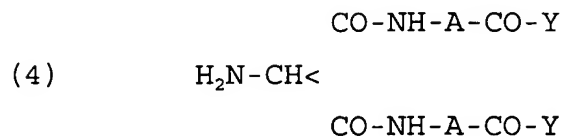


wherein, if N is present in R, X represents H, an Fmoc, Boc or Alloc group, and Y is OH or NH₂.

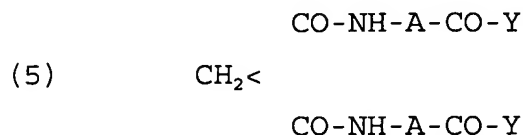
94. (Withdrawn) A ligand presenting assembly (LPA) having a formula selected from the group consisting of



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or



obtained by the method of claim 84, wherein A represents a peptide sequence having between 4 and 20 naturally occurring amino acid residues, and wherein Y represents OH or NH₂.

95. (Withdrawn) The method according to claim 85 for preparing an LPA selected from the group consisting of

[LPA-IV]: H-Lys-NHCH(CH₂CO-ProValValAlaGluSerProLysLysPro-OH)₂
(H-Lys-HNCH(CH₂CO-Seq. ID 1-OH)₂)

[LPA-XI]: Fmoc-AspProThrGlnAsnIleProProGly-NHCH(CH₂CO-
AspArgValTyrIleHisProPheHisLeu-NH₂)₂ (Fmoc-Seq. ID 6-
NHCH(CH₂CO-Seq. ID 5-NH₂)₂).